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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/080,471	02/22/2002	Helmut M. Sassenfeld	3091-A	8482

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EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/080,471	SASSENFELD ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,7,9-29,32,33,35-54 and 56-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,7,9-29,32,33,35-54 and 56-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/2/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

1. Claims 1-3, 6, 7, 9-29, 32, 33, 35-54 and 56-61 are pending in the instant application. Claims 25 and 52 have been amended as requested by Applicant in the Paper filed May 2, 2005. Claims 22-25 had been amended as requested by Applicant in the Paper filed July 28, 2004.

All claims are currently under examination.

Withdrawn Objections and Rejections

2. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-3, 6, 7, 9-29, 32, 33, 35-54 and 56-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of increasing the activity of the p75 TNF receptor produced by mammalian cells by contacting the receptor with a reduction/oxidation coupling reagent at a pH of about 7 to about 11 and isolating a fraction of the preparation of the recombinant soluble form of the p75 TNF receptor with a more active conformation, does not reasonably provide enablement for that method using the p55 TNF receptor. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification describes a series of experiments with p75 TNF:Fc, which elutes off a hydrophobic interaction column in three distinct peaks, in which fraction #2 binds TNF, and in which fraction #3 exhibits low TNF binding (Example1). Examples 2 and 3 describe disulfide exchange experiments with glutathione or L-cysteine, respectively, to drive p75 TNFR:Fc fraction #3 into the conformation of fraction #2. The treated proteins exhibited higher TNF binding activity after the treatments. However, there is no data supplied for any experiments with the p55 TNF receptor, which is significantly different from that of the p75 TNF receptor (less than 25% identical). See The Cytokine facts book, Second Edition, Academic Press, 2001, pages 476-478. It is not predictable that p55 TNF receptor produced recombinantly from mammalian cells would have different forms having unstable domains or less active conformations. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

It is acknowledged that the level of skill in the art is high. However, the prior art did not teach that a portion of mammalian proteins produced recombinantly in mammalian cells may not have the correct conformation and lower activity, and the specification has only provided a single working example, that of p75 TNF receptor. From the state of the prior art and a single

working example, it is not predictable that some of the p55 TNF receptor proteins produced recombinantly in mammalian cells would be of a different conformation. Therefore, the specification is enabling for the method of treatment of p75 TNF receptor, but not the p55 TNF receptor.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 27-29, 32, 33 and 35-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27 recites the limitation "**the** TNF-receptor" on line 2 of the claim. There is insufficient antecedent basis for this limitation in the claim, since there is more than one type of TNF receptor. The other claims are indefinite because they depend from claim 27.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-3, 6, 7, 9-29, 32, 33, 35-54 and 56-61 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3, 6, 7, 9-29, 32, 33, 35-54 and 56-61 remain indefinite because in the independent claims 1, 27 and 54 encompass methods of preparing and isolating a TNF receptor with a desired conformation, method of promoting a desired conformation of a TNF receptor and formulating into sterile unit dose form a TNF receptor that has been isolated from the TNF receptor with an undesired conformation. The claims do not specify what a desired or undesired conformation of a TNF receptor is or how such could be determined, and so it is not clear what is being claimed.

Applicants traverse the rejection at page 7-8 of the response and assert that one of ordinary skill in the art of recombinant protein production understands what is and is not a desired conformation of a recombinant protein, and point to the specification at page 3, lines 13-16, which states: "A desired conformation for a recombinant protein is the three-dimensional structure of a protein that most closely resembles, and/or duplicates the function of, the naturally occurring domain of that protein.

Applicants' arguments have been fully considered but are not deemed persuasive. Because the definition in the specification encompasses a protein that has a three-dimensional structure of a protein that duplicates the function of the claimed protein, it is not clear that the protein have the same sequence or structure, and may only have the same activity, so the claims are indefinite.

It is believed that all pertinent arguments have been answered.

Conclusion

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (571) 272-0829.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Publi c PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://portal.uspto.gov/external/portal/pair. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara

Eileen B. O'Hara, Ph.D.

Patent Examiner

EILEEN B. O'HARA
PATENT EXAMINER